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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,413	06/20/2006	Yoko Yamaguchi	WAS-NEG-P2/2F09028-US-P	8965

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EXAMINER	
PAK, JOHN D	

ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
07/16/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/595,413	YAMAGUCHI ET AL.	
	Examiner	Art Unit	
	John Pak	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-34* is/are pending in the application.

4a) Of the above claim(s) *22,23 and 29-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-21 and 24-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

Claims 1-17 have been canceled. Claims 18-34 are currently pending in this application.

Applicant's election of Group I in the reply filed on 4/12/2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 22, 23 and 29-34 are withdrawn from further consideration as being directed to non-elected subject matter. Claims **18-21** and **24-28** will presently be examined **to the extent** that they read on the elected subject matter.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed subject matter wherein the molar ratio of divalent metal halide or acetate to a carbonate or phosphate of an alkali metal is 1: (a number significant to provide sufficient carbonates) to 1:1.0, does not reasonably provide enablement for 1:0 or similarly low ratio. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The invention is directed to a coated retinoic acid microparticles but claim 20 specifically includes a ratio that reads on zero carbonate. However, if the carbonate amount is zero, there can be no divalent metal carbonate-coated retinoic acid. Therefore, the claim cannot be enabled for zero or small amount of carbonate (or phosphate). Claim language cannot explicitly recite non-enabled subject matter.

Claims 24-25 are objected to under 37 CFR 1.75 as being a substantial duplicate of claim 18. When two or more claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

It does not appear that claims 24-25 provide a further claim limitation to claim 18. Intended use ("for use") language of claims 24-25, without more, of a retinoic acid composition appears to cover the same subject matter as that of claim 18. Also, because the coated retinoic acid as set forth in claim 18 is already a sustained release retinoic acid composition, claim 24 appears to cover the same subject matter.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 18-21 and 24-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 02/096396 in view of Yamaguchi et al. (March 2002) and The Merck Index.

It is noted that U.S. Patent Application Publication 2004/0185113 (hereinafter, Mizushima et al.) is a 371 of the international application that published as WO 02/096396 in the Japanese language. Therefore, Mizushima et al. can serve as the English translation of WO 02/096396. ***All page or paragraph references hereinbelow are to said English translation of WO 02/096396***.

WO 02/096396 discloses encapsulating "a biologically active substance" with sparingly water-soluble calcium-containing inorganic microparticles such as calcium carbonate (paragraphs 0009 & 0015) by binding the active substance to the inside of the inorganic microparticles to provide slowing of active substance elution, i.e. sustained release, from the microparticles (paragraphs 0011 & 0016). The active substance should be capable of binding to calcium and is preferably negatively charged (paragraph 0013). The active substance includes low-molecular weight anticancer agents and various other active substance types (paragraph 0014). Preferred microparticle size is disclosed as 10 nm to 500 nm so that gaps in walls of blood vessels of cancer sites and other sites of interest can be passed through (paragraph 0016). "Altering the concentration of the inorganic matter, the concentration of the drug, the stirring speed, and the operating time and temperature control the size of the particles." (paragraph 0024). **In all the examples, a 1.3 to 1.0 molar ratio of calcium**

chloride to sodium carbonate was used. See paragraphs 0034 to 0051. Fine particle size of 10 nm can be produced by enhancing stirring power (id.). The microparticles are prepared by (1) preparing an aqueous solution of calcium salts such as calcium chloride, (2) adding and mixing an aqueous solution of a biologically active substance, and (3) adding and mixing an aqueous solution of carbonate such as sodium carbonate to allow the biologically active substance to be encapsulated (paragraph 0021). In order to prevent aggregation of microparticles, addition of protein, acid mucopolysaccharide, surfactant and mannitol to the reaction solution is taught (paragraph 0023; claim 14).

Yamaguchi et al.[1] disclose retinoid (e.g., all-trans retinoic acid, ATRA), as an essential lipophilic vitamin for growth, maintenance of vision, morphogenesis and normal differentiation of epithelial tissue, hematocytes and immunocompetent cells (page 1, first paragraph). ATRA forms micelles in aqueous solution, and a nanoparticulate core-shell structure in which calcium carbonate crystals were grown on the outer surface of the micelle is disclosed (page 1, first paragraph, lines 11-14). The ATRA-$CaCO_3$ formulation was prepared by gradual addition of $CaCl_2$ and $NaCO_3$ into the aqueous solution in which ATRA was previously allowed to form micelles. (page 1, second paragraph). The particles were hydrodynamically characterized as spherical particles with a diameter of approximately 125 to 164 nm (page 2, first paragraph).

[1] This document is in the Japanese language but applicant provided an English translation thereof. All references here are to the English translation.

The Merck Index is cited to establish that ATRA is a known antineoplastic agent (page 1414).

The difference between WO 02/096396 and the claimed invention is that WO 02/096396 does not explicitly disclose retinoic acid as the low-molecular weight active substance and that the average particle size of the encapsulated retinoic acid is 5 to 106.4 nm. However, the technology taught by WO 02/096396 for encapsulating "a biologically active substance" with sparingly water-soluble calcium carbonate by binding an active substance to the inside of the inorganic microparticles to provide sustained release from the microparticles is widely applicable to diverse active substances; and the secondary reference by Yamaguchi et al. is evidence that said technology would have been used to provide sustained release of retinoic acid. Not only is ATRA a well-known antineoplastic agent and thus suitable as an active substance in WO 02/096396, three of the inventors of WO 02/096396 later disclosed in the Yamaguchi et al. article the use of their encapsulating technology in encapsulating the water-insoluble ATRA.

Use of a surfactant in the reaction mixture is taught by WO 02/096396 as discussed above and specific choice of nonionic surfactant and common solvent such as lower alcohol would have been routine optimization to form suitable micelles of water-insoluble ATRA. The claimed ratio of halide to carbonate is actually taught by WO 02/096396 as already discussed above. The step of adjusting the average particle size to 5-106.4 nm would have been obvious for the benefit of passing through the walls

of blood vessels, as disclosed by WO 02/096396 (paragraph 0016), wherein increased stirring power has been taught for reducing to 10 nm (paragraph 0024).

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the teachings of the cited references.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 18-21 and 24-28 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 10/595,412. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

The copending claims are directed to substantially similar 5-106.4 nm average size retinoic acid nanoparticles comprising micelles of retinoic acid coated with an inorganic such as calcium carbonate (elected subject matter). The same production steps are disclosed in copending claims. For these reasons, one of ordinary skill in the art would have recognized the instant claimed invention as an obvious variation of the invention set forth in the copending claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to JOHN PAK whose telephone number is **(571)272-0620.** The Examiner can normally be reached on Monday to Friday from 8 AM to 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's SPE, Johann Richter, can be reached on **(571)272-0646**.

The fax phone number for the organization where this application or proceeding is assigned is **(571)273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/John Pak/
Primary Examiner, Art Unit 1616